

Applicant: Virginia Cornish
Serial No.: 10/056,874
Filed: January 24, 2002
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Listing of Claims

1-29. (Canceled)

30. (Currently Amended) A method for identifying a molecule that binds a known target receptor in a cell ~~from a pool of candidate molecules~~, comprising:

- (a) forming a screening molecule by covalently bonding each ~~the molecule in the pool of candidate molecules~~ to a ~~substrate comprising moiety~~ capable of selectively binding to and selectively forming a covalent bond with a receptor domain;
- (b) introducing the screening molecule into a cell culture comprising cells that express a first fusion protein of a LexA DNA-binding domain fused to a known target receptor domain ~~against which the candidate molecule is screened~~, a second fusion protein which comprises (i) a penicillin-binding-protein ("PBP") or a thymidine synthase ("TS") enzyme receptor domain capable of binding to and forming a the covalent bond with the screening molecule and (ii) a B42 transcription activation domain, and a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;
- (c) permitting the ~~the~~ screening molecule to bind to the first fusion protein and to the second fusion protein, bringing the two fusion proteins in to proximity so as to activate the expression of the reporter gene~~[[;]]~~;
- ~~(d) selecting the cell that expresses the reporter gene; and~~
- ~~(e) identifying the small molecule that binds the known target receptor wherein cellular expression of the reporter gene indicates that the molecule is able to bind to the known target receptor.~~

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31. (Previously Presented) The method of claim 30, wherein the cell is selected from the group consisting of insect cells, yeast cells, mammalian cells, and their lysates.
32. (Canceled).
33. (Canceled).
34. (Canceled).
35. (Currently Amended) The method of claim 34 30, wherein the PBP is the *Streptomyces* R61 PBP.
36. (Previously Presented) The method of claim 30, wherein the molecule is obtained from a combinatorial library.
37. (Currently Amended) The method of claim 30, wherein the steps (b)-(e c) of the method are iteratively repeated in the presence of a preparation of random ~~small~~ molecules for competitive binding with the screening molecule so as to identify a molecule capable of competitively binding the known target receptor.
38. (Currently Amended) A method for identifying ~~an unknown target~~ a target receptor as being able to bind to a ligand ~~to which a molecule is capable of binding in a cell~~ , comprising:
 - (a) providing a screening molecule having a ligand ~~which has a specificity for the unknown target receptor~~ covalently bonded to a ~~substrate~~ a moiety capable of selectively binding to and selectively forming a covalent bond with a second receptor;
 - (b) introducing the screening molecule into a cell which expresses

a first fusion protein of a LexA DNA-binding domain fused to the ~~unknown~~ target receptor domain ~~against which the candidate molecule is screened,~~

a second fusion protein which comprises (i) a penicillin-binding-protein ("PBP") or a thymidine synthase ("TS") enzyme second receptor domain capable of binding to and forming a the covalent bond with the screening molecule and (ii) and a B42 transcription activation domain, and

a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;

(c) permitting the screening molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene[[]],

~~(d) selecting which cell expresses the unknown target receptor; and~~

~~(e) identifying the unknown wherein cellular expression of the reporter gene indicates that the target receptor is able to bind to the ligand.~~

39. (Currently Amended) The method of claim 38, wherein the ~~unknown protein target~~ receptor is encoded by a DNA from the group consisting of ~~genomicDNA, cDNA and syntheticDNA~~ genomic DNA, cDNA and synthetic DNA.

40. (Previously Presented) The method of claim 38, wherein the ligand has a known biological function.

41-56. (Canceled)

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57. (New) The method of claim 30, wherein the chemical inducer of dimerization comprises a cephem or a fluorouracil moiety.
58. (New) The method of claim 38, wherein the substrate comprises a cephem or a fluorouracil moiety.